

CASE PH/58-19848/A/PCT/CONT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE APPLICATION OF

Art Unit: 1621

JALETT ET AL.

Examiner: S. Kumar

APPLICATION NO: 08/926,835

FAX RECEIVED

FILED: SEPTEMBER 10, 1997 FOR: PROCESS FOR THE HYDROGENATION OF IMINES

SEP 2.9 1998

Assistant Commissioner for Patents Washington, D.C. 20231

GROUP 1600

APPEAL BRIEF

Sir:

This is an ex parte appeal under 35 U.S.C. § 134 from the Office Action of December 22, 1997 (Paper No. 10) issued by Examiner, finally rejecting claims 1-37.

The Notice of Appeal and requisite appeal fee were mailed to the Patent and Trademark Office by first class mail with certificate of mailing on May 22, 1998, date stamped as received on May 26, 1998 making the brief due on July 26, 1998. This paper has been filed within four (4) months from the date of the of Notice of Appeal. A Petition for a two-month extension of time for filing this appeal brief along with the requisite fee are submitted concurrently herewith. Appellants' response and fee payment has been filed in accordance with 35. U.S.C. § 21 and 37 CFR § 1.7.

(1) Real party in interest.

The invention disclosed herein has been assigned to Ciba-Geigy Corporation now renamed as Novartis Corporation, a New York Corporation.

Novartis Corporation is wholly owned subsidiary of Novartis AG.

(2) Related appeals and interferences.

No other related appeals or interferences are known to Appellant.

(3) Status of the Claims.

Claims 1-37 were originally filed.

The claims on appeal, 1-37, stand finally rejected under 35 USC § 102 (claims 1-35) and § 103 (claims 1-37).

A clear copy of the appealed claims 1-37 appears in the Appendix.

(4) Status of the Amendments.

The claims were not amended in response to the final rejection.

(5) Concise Summary of the Invention.

As shown on page 1, last paragraph, of the present application the present invention relates to a process for the hydrogenation of imines with hydrogen under elevated pressure in the presence of iridium catalysts and with or without an inert solvent, wherein the reaction mixture contains an ammonium chloride, bromide or iodide, or a metal chloride, bromide or iodide that is soluble in the reaction mixture, the metal preferably being an alkali metal, and additionally contains an acid. (emphasis supplied)

(6) Issues.

Two issues are presented for review.

- (a). WHETHER CLAIMS 1-35 ARE ANTICIPATED UNDER 35 USC § 102 BY THE DISCLOSURE IN U.S. PATENT 5,112,999 TO OSBORN ET AL.
- (b). WHETHER CLAIMS 1-37 ARE OBVIOUS UNDER 35 USC § 103 OVER THE COMBINED DISCLOSURES OF U.S. PATENTS 5,112,999 (Osborn et al.), 5,426,223 (Burk), 5,103,061 (Blackborow et al.) and 5,210,202 (Petit et al.) and Chao et al., Tetrahedron Asymmetry Vol. 3, No. 3, pp. 337-340, 1992.

(7) Grouping of Claims.

The claims do not stand or fall together with regard to issue (a). Claims 1-27, 31-33 and 35 are process claims that are argued separately from claims 28, 29, 30 and 34 which each contain specific limitations which have not heretofore been addressed by the Examiner.

Likewise, the claims do not stand or fall together with regard to issue (b). 1-27 and 35-37 are process claims that are argued separately from claims 28, 29, 30 and 34 which each contain specific limitations which have not heretofore been addressed by the Examiner.

(8) Argument.

Appellants base this appeal upon error which is apparent in the Examiner's interpretation of the applied references.

(a). WHETHER CLAIMS 1-35 ARE ANTICIPATED UNDER 35 USC § 102 BY THE DISCLOSURE IN U.S. PATENT 5,112,999 TO OSBORN ET AL.

Claims 1-35 have been finally rejected under § 102(b) as being anticipated by the disclosure of U.S. patent 5,112,999 issued to Osborn et al (collectively "Osborn").

Osborn is cited and distinguished in the background description of the instant application on page 1 thereof. Appellants respectfully submit that there is insufficient evidence in the cited reference to support the Examiners position that claims 1-35 are anticipated.

In the final rejection, the Examiner states that Osborn "anticipates [the] instant process in terms of catalyst, solvent, temperature, and metal salt, along with [the] type of the compounds being hydrogenated." However, Appellants note that Osborn is totally silent with respect to an iridium catalyzed hydrogenation reaction that "additionally contains an acid" as required by the present claims. Accordingly, claims 1-35 are novel over Osborn and not at all anticipated by its teaching. To the contrary, Osborn only employs alkaline metal or ammonium halides in the process (see column 6, lines 49 to 54).

Moreover, no ingredients are present in the reaction mixture of Osborn which could generate an additional acid during the hydrogenation process. Contrary to the Examiner's implication in the June 3rd Advisory action, the disclosure of -SO₃H as a substituent of the disphosphine ligand of the iridium catalyst does <u>not</u> constitute a disclosure of an iridium catalyzed hydrogenation reaction that "additionally contains an acid." Accordingly, the § 102 rejection of claims 1-35 over the disclosure of Osborn et al. is in error and should be reversed.

(a-1). Whether Claims 28, 29, 30 and 34 are Anticipated by Osborn et al.

Even if claims 1-27, 31-33 and 35 are found to be anticipated, claims 28, 29, 30 and 34 are novel over the disclosure of Osborn et al. due to the specific limitations contained therein. More particularly, such claims specify further parameters and limitations for the hydrogenation process of claim 1 which are neither disclosed nor even remotely suggested by Osborn et al. A proper

anticipation rejection requires that all of the limitations of a claim be described in the cited reference.

Osborn et al contains no teaching with respect to:

- the specific amounts of the additional acid reagent (by weight, based on the imine) that are required by claim 28;
- the specific additional acid reagents required by claims 29-30; and
- a hydrogenation process of claim 1 that is carried out in a loop reactor as required in claim 34.

Accordingly, claims 28, 29, 30 and 34 are not anticipated by the disclosure of Osborn et al. and the rejection of the Examiner should be reversed.

(b). WHETHER CLAIMS 1-37 ARE OBVIOUS UNDER 35 USC § 103 OVER THE COMBINED DISCLOSURES OF U.S. PATENTS 5,112,999 (Osborn et al.), 5,426,223 (Burk), 5,103,061 (Blackborow et al.) and 5,210,202 (Petit et al.) and Cho et al., Tetrahedron Asymmetry Vol. 3, No. 3, pp. 337-340, 1992.

The distinctions between Osborn and the appealed claims are discussed above. Appellants submit that the disclosures of Burk, Blackborow et al., Petit et al. and Cho et al. (the "secondary references") do not remedy the deficiencies of Osborn et al. More specifically, none of the secondary references teach or suggest that an additional acid reagent should be employed in Osborn et al.'s iridium catalyzed hydrogenation process.

Burk neither discloses the addition of halide for the hydrogenation nor the addition of a metal or ammonium halide. The halide mentioned in the abstract is used to cleave the N-N bond of the hydrozones obtained by the hydrogenation in separate reaction. Furthermore, the catalyst used in example 1, line 39, of Burk (noted by the Examiner in the June 3rd Advisory) employs a rhodium complex salt with a CF₃SO₃ anion. No acid is added to the reaction mixture!

Petit et al. discloses some chiral ligands with amine and phosphine moieties not encompassed by the term diphosphines as used in the present claims. The compounds are used as ligands in hydrogenation catalysts. Petit et al. does not contain even the slightest hint with respect to the additional use of an acid. Thus, the instant process is well distinguished from Petit et al. by the presence of a halide and an acid.

Blackborow et al. disclose the hydrogenation of imines with metal catalysts like platinum on carbon. There is no teaching or suggestion regarding the use of an additional acid reagent. In

addition, halides are not present in the reaction mixture. Accordingly, even if combined with Osborn et al., such combination would not result in the presently claimed invention.

Cho et al. use boron hydrides with chiral ligands as catalysts and neither add an acid nor a metal or ammonium halide to the hydrogenation process. The Examiner appears to confuse the manufacture of the imine 2, where catalytic amounts of p-toluenesulphonic acid are added (second line under formula 8 therein), with the subsequent hydrogenation process. The hydrogenation (reduction procedure) of imine 2 with hydrides (not hydrogen) is carried out without acid (p. 338., third line under formula 8).

Accordingly, it appears that the Examiner has failed to appreciate the invention and cites therefore prior art which bears only a superficial relevance, but does not render obvious the claimed process. Moreover, the cited prior art does not show that activity of (known catalysts as for example described by Osborn) is increased, deactivation is reduced or eliminated, and additionally, enantioselectivity is high even at higher reaction temperatures (See page 1, paragraph 4 of the instant specification), when the reaction mixture to be hydrogenated additionally contains an acid.

Appellants submit that a consideration of the invention as a whole affirmatively involves taking into account the above-noted results and advantages produced by the claimed process. To have ignored such considerations was an error on the part of the Examiner. Accordingly, the Examiner's rejection of claims 1-37 as being obvious over the above-cited prior art should be reversed.

(b-1). Whether Claims 28, 29, 30 and 34 are Obvious over Osborn et al. and the Secondary References

Even if claims 1-27, 31-33 and 35-37 are found to be *prima facie* obvious, claims 28, 29, 30 and 34 are nonobvious over the disclosure of Osborn et al. and the secondary references due to the specific limitations contained therein. More particularly, such claims specify further parameters and limitations for the hydrogenation process of claim 1 which are neither disclosed nor even remotely suggested by Osborn et al. taken alone or in any combination with the secondary references. A consideration of the invention as a whole affirmatively involves taking into account such claim limitations (which are outlined in (a-1) above). In light of such limitations, claims 28, 29, 30 and 34 are not *prima facie* obvious over the disclosures of Osborn et al. and the secondary references. Accordingly, the rejection of the Examiner should be reversed.

For the reasons above, Appellants respectfully submit that all rejections of claims 1-37 under §§ 102-103 over the disclosures of Osborn et al. and the secondary references are in error as to fact and law and should be reversed.

If any fee under 37 CFR § 1.17 is due in connection with this Appeal Brief, the Commissioner is authorized to charge Deposit Account No. 19-0134 for the appropriate amount.

Respectfully submitted.

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Date: September 28, 1998

ENCL. APPENDIX (9 pp.)

Petition for two-month extension

Fee Letter

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APPENDIX

WHAT IS CLAIMED IS:

- 1. A process for the hydrogenation of an imine with hydrogen under elevated pressure in the presence of an iridium catalyst and with or without an inert solvent, wherein the reaction mixture contains an ammonium chloride, bromide or iodide, or a metal chloride, bromide or iodide that is soluble in the reaction mixture, and additionally contains an acid.
- 2. A process according to claim 1, wherein the imine contains at least one N—group.
- 3. A process according to claim 1, wherein the imine contains at least one of the groups

 C=N- and C=N-N- and additionally unsaturated groups

 C=O.
- 4. A process according to claim 3, wherein the free bonds are saturated with hydrogen or organic radicals having from 1 to 22 carbon atoms or organic hetero radicals having from 1 to 20 carbon atoms, and at least one hetero atom from the group O, S, N and P; or the nitrogen atom of the group N— is saturated with NH_2 or a primary amino group having from 1 to 22 carbon atoms or a secondary amino group having from 2 to 40 carbon atoms.
- 5. A process according to claim 1, wherein an aldimine, ketimine or hydrazone is hydrogenated.
- 6. A process according to claim 5, wherein the imine is an imine of formula I

$$\begin{array}{c}
R_1 \\
R_2
\end{array}$$
(1),

which is hydrogenated to form an amine of formula II

$$\begin{array}{c}
R_1 \\
CH - NH - R_3
\end{array}$$
(II)

wherein

 R_3 is linear or branched C_1 - C_{12} alkyl, cycloalkyl having from 3 to 8 ring carbon atoms; heterocycloalkyl bonded via a carbon atom and having from 3 to 8 ring atoms and 1 or 2 hetero atoms from the group O, S and NR_6 ; a C_7 - C_{16} aralkyl bonded via an alkyl carbon atom, or C_1 - C_{12} alkyl substituted by the mentioned cycloalkyl or heterocycloalkyl or heteroaryl;

or wherein

 R_3 is C_6 - C_{12} aryl, or C_4 - C_{11} heteroaryl bonded via a ring carbon atom and having 1 or 2 hetero atoms in the ring; R_3 being unsubstituted or substituted by -CN, -NO₂, F, Cl, C_1 - C_{12} alkyl, C_1 - C_{12} alkoxy, C_1 - C_{12} alkylthio, C_1 - C_6 haloalkyl, -OH, C_6 - C_{12} -aryl or -aryloxy or -arylthio, C_7 - C_{16} -aralkyl or -aralkoxy or -aralkylthio, secondary amino having from 2 to 24 carbon atoms, -CONR₄R₅ or by -COOR₄, and the aryl radicals and the aryl groups in the aralkyl, aralkoxy and aralkylthio in turn being unsubstituted or substituted by -CN, -NO₂, F, Cl, C_1 - C_4 -alkyl, -alkoxy or -alkylthio, -OH, -CONR₄R₅ or by -COOR₄; R_4 and R_5 are each independently of the other hydrogen, C_1 - C_{12} alkyl, phenyl or benzyl, or R_4 and R_5 together are tetra- or penta-methylene or 3-oxapentylene;

 R_6 has independently the same meaning as given for R_4 ; R_1 and R_2 are each independently of the other a hydrogen atom, C_1 - C_{12} alkyl or cycloalkyl having from 3 to 8 ring carbon atoms, each of which is unsubstituted or substituted by -OH, C_1 - C_{12} alkoxy, phenoxy, benzyloxy, secondary amino having from 2 to 24 carbon atoms, -CONR₄R₅ or by -COOR₄; C_6 - C_{12} aryl or C_7 - C_{16} aralkyl that is unsubstituted or substituted as R_3 , or -CONR₄R₅ or -COOR₄, wherein R_4 and R_5 are as defined hereinbefore; or

 R_3 is as defined hereinbefore and R_1 and R_2 together are alkylene having from 2 to 5 carbon atoms that is optionally interrupted by 1 or 2 -O-, -S- or -NR₆- radicals, and/or unsubstituted or substituted by =O or as R_1 and R_2 above in the meaning of alkyl, and/or condensed with benzene, pyridine, pyrimidine, furan, thiophene or pyrrole; or

 R_2 is as defined hereinbefore and R_1 and R_3 together are alkylene having from 2 to 5 carbon atoms that is optionally interrupted by 1 or 2-O-, -S- or -NR₆- radicals, and/or

unsubstituted or substituted by =0 or as R_1 and R_2 above in the meaning of alkyl, and/or condensed with benzene, pyrimidine, furan, thiophene or pyrrole.

- 7. A process according to claim 5, wherein R_1 and R_2 as heteroaryl form a 5- or 6-membered ring having 1 or 2 identical or different hetero atoms.
- 8. A process according to claim 5, wherein R_1 and R_2 as heteroaryl-substituted alkyl are derived from a 5- or 6-membered ring having 1 or 2 identical or different hetero atoms.
- 9. A process according to claim 5, wherein R_1 and R_2 as heterocycloalkyl or as heterocycloalkyl-substituted alkyl contain from 4 to 6 ring atoms and 1 or 2 identical or different hetero atoms from the group O, S and NR₆, wherein R₆ is hydrogen, C_1 - C_{12} alkyl, phenyl or benzyl.
- 10. A process according to claim 5, wherein R_1 , R_2 and R_3 as alkyl are unsubstituted or substituted C_1 - C_6 alkyl.
- 11. A process according to claim 5, wherein R_1 , R_2 and R_3 as unsubstituted or substituted cycloalkyl contain from 3 to 6 ring carbon atoms.
- 12. A process according to claim 5, wherein R_1 , R_2 and R_3 as are unsubstituted or substituted naphthyl or phenyl, and R_1 , R_2 and R_3 as aralkyl are unsubstituted or substituted phenylalkyl having from 1 to 10 carbon atoms in the alkylene.
- 13. A process according to claim 5, wherein R_1 and R_2 together or R_1 and R_3 together form, with the carbon atom or the -N=C group to which they are bonded, respectively, a 5-or 6-membered ring.
- 14. A process according to claim 5, wherein in formula I R_3 is 2,6-di- C_1 - C_4 alkylphen-1-yl, R_1 is C_1 - C_4 alkyl, and R_2 is C_1 - C_4 alkyl, C_1 - C_4 alkoxymethyl or C_1 - C_4 alkoxyethyl.
- 15. A process according to claim 14, wherein R_3 is 2,6-dimethylphen-1-yl or 2-methyl-6-ethylphen-1-yl, R_1 is ethyl or methyl, and R_2 is methoxymethyl.
- 16. A process according to claim 6, wherein the imine corresponds to the formula

$$\begin{array}{c|c} \text{CH}_3 & \text{N} = \text{C} - \text{CH}_2\text{OCH}_3 \\ \text{CH}_3 & \text{(Vc)}. \end{array}$$

- 17. A process according to claim 1, wherein the iridium catalyst is a homogeneous catalyst that is substantially soluble in the reaction medium.
- 18. A process according to claim 1, wherein the catalyst corresponds to the formula III, IIIa, IIIb, IIIc or IIId

[XIrYZ] (III),

[YIrZ₄][⊖]M[⊕] (IIIb).

[YIrHZ₂]₂ (IIIc),

 $[YIrZ_3]_2$ (IIId),

wherein X is two olefin ligands or a diene ligand, Y is a diphosphine having secondary phosphine groups

- (a) the phosphine groups of which are bonded to a carbon chain having from 2 to 4 carbon atoms, or
- (b) the phosphine groups of which are either bonded directly or via a bridge group
- -CR_aR_b- in the ortho positions of a cyclopentadienyl ring or are each bonded to a cyclopentadienyl ring of a ferrocenyl, or
- (c) one phosphine group of which is bonded to a carbon chain having 2 or 3 carbon atoms and the other phosphine group of which is bonded to an oxygen atom or a nitrogen atom bonded terminally to that carbon chain, or
- (d) the phosphine groups of which are bonded to the two oxygen atoms or nitrogen atoms bonded terminally to a C_2 -carbon chain;

with the result that in the cases of (a), (b), (c) and (d) a 5-, 6- or 7-membered ring is

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formed together with the Ir atom, the radicals Z are each independently of the other(s) Cl. Br or I, A^{\ominus} is the anion of an oxy or complex acid, and M^{\ominus} is an alkali metal cation or quaternary ammonium, and R_a and R_b are each independently of the other hydrogen, C_1 - C_8 alkyl, C_1 - C_4 fluoroalkyl, phenyl or benzyl or are phenyl or benzyl having from 1 to 3 C_1 - C_4 alkyl or C_1 - C_4 alkoxy substituents.

- 19. A process according to claim 18, wherein the diphosphine Y contains at least one chiral carbon atom.
- 20. A process according to claim 18, wherein X as an olefin ligand is branched or linear C_2 - C_{12} alkylene; and X as a diene ligand is an open-chain or cyclic diene having from 4 to 12 carbon atoms.
- 21. A process according to claim 18, wherein the secondary phosphine groups contain two identical or different radicals from the following group: linear or branched C_1 - C_{12} alkyl; unsubstituted or C_1 - C_6 alkyl- or C_1 - C_6 alkoxy-substituted C_5 - C_{12} cycloalkyl, C_5 - C_{12} cycloalkyl- CH_2 -, phenyl or benzyl; or phenyl or benzyl substituted by halogen (e.g. F, Cl or Br), C_1 - C_6 haloalkyl, $(C_1$ - C_{12} alkyl)₃Si, $(C_6H_5)_3$ Si, C_1 - C_6 haloalkoxy (e.g. trifluoromethoxy), -NH₂, phenyl₂N-, benzyl₂N-, morpholinyl, piperidinyl, pyrrolidinyl, $(C_1$ - C_{12} alkyl)₂N-, -ammonium- X_1 - C_1 - C_2 - C_3 - C_4 - C_5 - C_4 - C_5 - $C_$
- 22. A process according to claim 18, wherein the diphosphine Y is of the formula:

wherein

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 R_{15} and R_{16} are each independently of the other hydrogen, C_1 - C_4 alkyl, phenyl, benzyl, or phenyl or benzyl having from 1 to 3 C_1 - C_4 alkyl or C_1 - C_4 alkoxy substituents,

 R_{14} is hydrogen, C_1 - C_4 alkyl, phenyl, benzyl, or phenyl or benzyl having from 1 to 3 C_1 - C_4 alkyl or C_1 - C_4 alkoxy substituents,

 R_{17} is hydrogen, C_1 - C_4 alkyl, phenyl, benzyl, C_1 - C_6 alkoxy-CO-, C_1 - C_6 alkyl-CO-, phenyl-CO-, naphthyl-CO- or C_1 - C_4 alkylNH-CO-,

A may be identical or different groups -PR₂, wherein R is C_1 - C_6 alkyl, cyclohexyl, phenyl, benzyl, or phenyl or benzyl having from 1 to 3 C_1 - C_4 alkyl, C_1 - C_4 alkoxy, -CF₃ or partially or fully fluorinated C_1 - C_4 alkoxy substituents, and

n is 0, 1 or 2.

- 23. A process according to claim 18, wherein the diphosphine Y is
- ((R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-phenyl)phosphine
- ((R)-1-[(S)-2-diphenylphosphino)ferrocenyl])ethyl-di(3,5-dimethyl-4-N,N-dipropylaminophenyl)phosphine
- $\{(R)-1-[(S)-2-diphenylphosphino) ferrocenyl]\} ethyl-di(3,5-diisopropyl-4-N,N-dimethyl-aminophenyl) phosphine \\$
- {(R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-diisopropyl-4-N,N-dibenzylyl-aminophenyl)phosphine
- {(R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-4-N,N-dibenzylylaminophenyl)phosphine
- ((R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-4-(1'-pyrrolo)-phenyl)phosphine
- {(R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-4-N,N-dipentyl-aminophenyl)phosphine
- [(R)-1-[(S)-2-diphenylphosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-4-N,N-dimethyl-aminophenyl)phosphine
- 1,4-bis(diphenylphosphino)butane or
- [(R)-1-[(S)-2-di(4-methoxyphenyl)phosphino)ferrocenyl]}ethyl-di(3,5-dimethyl-
- 4-N,N-dimethylaminophenyl)phosphine.
- 24. A process according to claim 1, wherein the ammonium chloride, bromide or iodide, or the metal chloride, bromide or iodide that is soluble in the reaction mixture, is used in an amount of from 0.01 to 200 mol %, based on the iridium catalyst.
- 25. A process according to claim 1, wherein the metal chloride, bromide or iodide used is an alkali metal chloride, bromide or iodide.
- 26. A process according to claim 1, wherein the ammonium or alkali metal chloride, bromide or iodide is a tetraalkylammonium chloride, bromide or iodide having from 1 to 6 carbon atoms in the alkyl groups or in the case of an alkali metal chloride, bromide or iodide is a sodium, lithium or potassium chloride, bromide or iodide.
- 27. A process according to claim 1, wherein the acid is an inorganic or organic acid.

- 28. A process according to claim 1, wherein the acid is used in an amount of from 0.001 to 50 % by weight, preferably 0.1 to 50 % by weight, based on the imine.
- 29. A process according to claim 27, wherein the organic acid is an aliphatic or aromatic carboxylic acid, sulfonic acid or phosphorus(V) acid.
- 30. A process according to claim 27, wherein the organic acid is acetic acid, propionic acid, trifluoroacetic acid, chloroacetic acid or methanesulfonic acid, and the inorganic acid is $\rm H_2SO_4$.
- 31. A process according to claim 1, wherein the molar ratio of the imine to the iridium catalyst is from 500 000 to 20.
- 32. A process according to claim 1, wherein the reaction temperature is from -20 to 100°C.
- 33. A process according to claim 1, wherein the hydrogen pressure is from 5 to 150 bar.
- 34. A process according to claim 1, wherein the hydrogenation is carried out in a loop reactor.
- 35. A process according to claim 1, wherein an aldimine or a ketimine formed in situ before or during the hydrogenation is hydrogenated.
- 36. A process for the preparation of a compound of the formula

CICH₂CO
$$R_{03}$$
 R_{04} R_{02} R_{01} R_{01} (IV),

wherein R_{01} , R_{02} and R_{03} are each independently of the other C_1 - C_4 alkyl, and R_{04} is C_1 - C_4 alkyl or C_1 - C_4 alkoxymethyl or C_1 - C_4 alkoxyethyl, by (1) hydrogenation of an imine of the formula

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$$R_{03} \subset R_{04}$$

$$R_{02} \longrightarrow R_{01}$$

$$R_{01} \qquad (V)$$

with hydrogen in the presence of an iridium catalyst and with or without an inert solvent to form an amine of the formula

and (2) reaction thereof with the compound of formula

wherein in the hydrogenation the reaction mixture contains an ammonium chloride, bromide or iodide, or a metal chloride, bromide or iodide that is soluble in the reaction mixture, and additionally contains an acid.

37. A process according to claim 36, wherein the imine used is a compound of the formula

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